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Archimedes: Can fetal echocardiograms reliably predict the need for urgent Balloon Atrial Septostomy in Transposition of the Great Arteries?

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Clinical scenario

A term neonate is admitted to the neonatal unit with an antenatal diagnosis of transposition of the great arteries with intact ventricular septum (TGA/IVS) and a 6mm patent foramen ovale, identified by fetal echocardiogram at 34 weeks gestational age. The pre and post-ductal oxygen saturations (SpO_2) are 45% and 55% in 100% oxygen. Prostaglandin therapy is commenced at 5 ng/kg/min. In view of unresponsive hypoxaemia, the baby is intubated, mechanically ventilated, and prostaglandin dose is escalated to 50 ng/kg/min. However, little improvement in oxygen saturations is noted. You then question the need for urgent Balloon Atrial Septotomy (BAS) although fetal echocardiogram suggested adequate mixing at the atrial connection.

Structured Clinical question

In neonates, with an antenatal diagnosis of TGA with IVS or small VSD (patient), can fetal echocardiogram (intervention) predict the need for urgent BAS (outcome)?

Search

Cochrane, Medline, Embase, Cinahl and Maternity and infant care databases were searched on 6 March 2019. The following terms were used: exp ''INFANT, NEWBORN''/ OR (newborn * OR neonates*) AND exp ''HEART DETECTS, CONGENITAL''/ OR (congenital heart AND (defect* OR malformation*)) AND exp "ULTRASONOGRAPY, PRENATAL''/ OR ((prenatal OR antenatal) AND (ultrasonography OR ultrasound OR scan)) OR (echocardiogram OR echocardiograph*, OR ''cardiac echo'') AND exp FETUS/OR exp ''FETAL RESEARCH''/ OR ((fetal OR foetal OR fetus OR foetus OR prenatal OR antenatal) AND echocardiog*) AND (''Balloon atrial septostomy '' OR atrial septostomy), OR Balloon atrial septostomy OR atrioseptostomy). In total, 31 publications were identified, in which 4 studies were relevant on further review[1-4]. All four studies included newborns with an antenatal diagnosis of TGA.

Commentary

Congenital heart defects (CHD) are the most common congenital anomaly affecting approximately 8 per 1,000 livebirths[5]. Data from the National Institute for Cardiovascular Outcomes Research (NICOR-Congenital) shows improving antenatal CHD detection rates across England, with an increase in antenatal diagnoses of TGA/IVS from 27.2% in 2007 to 66.7% in 2016[6]. This correlates with the introduction of routine screening of outflow tracts to the NHS Fetal Anomaly Screening Programme recommended by the National Institute of Health and Clinical Excellence[7].

TGA accounts for 5-7% of all CHD[8]. The survival of neonates with TGA has improved following adoption of new cardiac surgical techniques and enhanced postoperative management[9]. Antenatal detection, allowing for planned delivery in experienced tertiary centres and improved early neonatal management has also

improved outcomes[10, 11]. Despite these advances, some neonates with known TGA will show profound hypoxaemia after birth, secondary to inadequate circulatory mixing, which can led to preoperative mortality and morbidity[12]. BAS is an accepted standard treatment. It creates an adequate inter-atrial communication allowing satisfactory oxygenation of the systemic blood, thereby stabilising patients prior to surgery[13]. However predicting which patients will need an urgent BAS on fetal echocardiogram is challenging. BAS is performed in presence of significant hypoxaemia (pre-ductal saturations ≤ 70 %), despite prostaglandin therapy and invasive ventilatory support, with echocardiographic demonstration of restrictive inter-atrial communication preventing circulatory mixing[1-4].

From our literature search, only one retrospective cohort study[1] was identified which compared fetal echocardiographic markers in isolated TGA and gestation-matched fetuses to predict the need for urgent BAS. This was a single-centre study with an appropriate control population, although the study cohort was small (n=80). The study found the ratio of Foramen Ovale (FO) to Total Septal length was significantly smaller in those who required an urgent BAS. Other parameters including arterial duct, pulmonary valve or branch pulmonary artery diameters were not significantly different in study groups. A hypermobile and/or aneurysmal atrial septum were also noted in normal fetuses and those with TGA and did not predict need for urgent BAS.

Three other retrospective case-series studies that examined possible predictors of urgent BAS using different fetal echocardiography markers in neonates with TGA were identified. Tuo *et al.* [2] demonstrated restrictive FO or hypermobile or redundant septum primum was significantly associated with need for urgent BAS. Punn *et al.* [3] also examined the morphology and function of FO, and ductal size and shunting pattern. They found a hypermobile septum and reverse diastolic DA had a significant association with urgent BAS. Jouannic *et al.*[4] examined the size of the FO and DA to determine the specificity and sensitivity for urgent BAS. They concluded that a restricted FO and/or constricted DA had a specificity of 84%, to predict the need for urgent BAS, but a low sensitivity of 31%.

In conclusion, all identified studies were retrospective and single centred with small sample sizes. The individual markers in each study were not universally present in all affected cases, making the interpretation of the results challenging. The findings of each study were variable, with contradictory conclusions. With the lack of evidence to make reliable prediction of need for BAS on fetal echocardiograms, neonates with TGA and IVS or small VSD should be delivered in centres with emergency interventional cardiology support, should there be an urgent need for intervention. For those neonates delivered inadvertently in neonatal units with no interventional cardiology services, there should be an urgency of transferring to a cardiology center, following commencement of prostaglandin therapy.

Clinical bottom line

- There are no consistent markers on fetal echocardiography that reliably predict need for BAS in TGA (Grade D)

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Table 1:

Citation	Study Group	Study Type	Outcomes	Key Results	Comments
Vigneswaran et al[1]	40 neonates with isolated TGA compared to 40 gestation-matched neonates. 12 neonates with TGA had urgent BAS.	Retrospective cohort study	To predict need for urgent BAS with prenatal echocardiographic markers: • foramen ovale length(FO) • FO: Total Septal length (TSL) ratio • Arterial valves, branch pulmonary arteries (PA) and arterial duct measurements • Atrial septum (AS) flap valve appearance: aneurysmal, fixed, hypermobile or normal	• FO length and FO: TSL similar in normal fetuses and in TGA group not requiring urgent BAS • Urgent BAS group had smaller FO length (p 0.005) and FO:TSL (p =0.001) (S) • All cases (3) with limited AS movement required BAS • Hypermobile AS not associated with need for urgent BAS • Arterial duct, pulmonary valve, or branch PA diameters not significantly different between urgent BAS and other groups	Likelihood of an emergency BAS increased by FO:TSL <0.5 and a fixed appearance of the AS flap valve.
Tuo G et al	40 neonates with antenatal d-TGA of which 20 neonates had urgent BAS	Retrospective case series	To evaluate correlation between need for urgent BAS and antenatal appearance of the AS/ foramen ovale (FO), ductus arteriosus (DA) and pulmonary veins (PV)	• All neonates with antenatal restrictive FO (=9) required an urgent BAS (p< 0.0001) (S) • 5/8 neonates with antenatal hypermobile FO, and 6/8 fetuses with a redundant FO appearance required an urgent BAS (p= 0.002 and 0.0001 respectively) (S)	The challenges of the prenatal evaluation of FO morphology for accurate prediction of need for urgent BAS were highlighted.

Punn et al	26 neonates with complete TGA, sub-grouped into urgent (within a few hours after birth) BAS (=14) or non-urgent BAS (=12).	Retrospective case series	To identify foetal predictors for need for an emergency BAS	• Antenatal Hypermobile AS was associated with an urgent BAS (P = .0007, specificity and PPV 1) (S), however the sensitivity and NPV were only 0.64 and 0.71 respectively • Antenatal reverse diastolic ductal shunt was associated with an urgent BAS (P = .0145, specificity of 0.92 and PPV of 0.89) (S); however, the sensitivity and NPV were 0.57 and 0.65, respectively	The hypermobile AS and diastolic reverse ductal shunt are promising predictors for need of urgent BAS.
Jouannic et al.	130 neonates with antenatal diagnosis of TGA. 108 neonates had TGA with an intact ventricular septum (IVS) or small VSD	Retrospective case series	To determine the specificity and sensitivity of a restricted FO and/ or constricted DA in predicting need for urgent BAS	• Specificity of restricted FO or constricted DA to predict urgent BAS was 84% while sensitivity was 54% •The specificity of both FO and DA restriction to predict urgent BAS was 100% (S), but the sensitivity was 31% •6/95 neonates who were considered to have a normal foetal prenatal shunts, required urgent BAS	Presence of restricted FO and DA constriction helps to predict need for urgent BAS but absence of the above does not rule out need for urgent BAS.

NS = Non-significant, S = Significant